Therapeutic Controversy

The Ischemic Tolerance of Neural Tissue and the Need for Monitoring and Selective Shunting During Carotid Endarterectomy

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DR. FERGUSON'S RECENT provocative editorial on the subject of monitoring and shunting during carotid endarterectomy was both puzzling and troubling. It appears that his "inescapable conclusion that neither intraoperative monitoring nor the use of internal shunts are necessary to avoid intraoperative stroke in the carotid endarterectomy, as a usual cause for such a stroke is an embolus" was based largely on: a comparison of reported series, his own experience with the use of intraoperative electroencephalography and cerebral blood flow measurements, and his interpretation of clinical and laboratory studies concerning the ischemic tolerance of neural tissue. He recommends "skillful general anesthesia together with a relatively short occlusion time" as the preferred method of management. These components of his thesis will be considered sequentially.

Comparing Reported Operative Series

A comparison of surgical series according to the method of protection used at surgery is interesting but is probably an exercise of limited usefulness. Major differences in patient populations, the indications for surgery, methods of patient evaluation prior to and following surgery, the completeness and accuracy of case records, and the presence or absence of an active role by a neurologist in the detailed preoperative and postoperative neurological evaluation of the cases makes such an analysis extraordinarily difficult. Of special importance among these differences are the indications for carotid artery surgery. The management of the asymptomatic carotid plaque is controversial with sound arguments on both sides of the issue. However, in some institutions, the major indication for surgery is a carotid plaque, with or without neurological complaints, while in others the primary indication remains focal neurological symptoms. This introduces a major bias in the comparison of various reports.

The bearing of risk factors has not only been documented by a number of studies, but is simply a matter of common sense. Elective surgery in a 55-year-old patient with an asymptomatic unilateral carotid stenosis who is in good health and without medical and neurological risk factors cannot be compared to that of emergency surgery in an obese 70-year-old patient with an ipsilateral stenosis and contralateral occlusion who is a heavy smoker with obstructive pulmonary emphysema, diabetic, actively symptomatic from coronary artery disease, and having crescendo transient ischemic attacks not controlled by heparin. One might reasonably expect a 1% risk of surgery in the former patient but not in the latter. In fact, the risk of surgery in the latter group has led some observers, examining only surgical statistics, to advise against surgery in this type of patient. Yet, successful surgery in this latter case can be most dramatic and effective in altering the natural history of the illness. It is in this type of patient that monitoring techniques are particularly important and in whom shunting most frequently has been required.

Operative and Postoperative Strokes

In order, presumably, to facilitate a comparison of these series and to place in perspective the reported stroke rates, Dr. Ferguson identified the stroke rate as intraoperative in those in which this information could be extracted (in this regard it should be noted that our total perioperative major and minor morbidity was incorrectly quoted as intraoperative). Actually, a breakdown into intraoperative, postoperative, or perioperative (operative and within 30 days thereafter) is useful but not mandatory, as a stroke during surgery or in the postoperative period has a similar significance if the latter occurred because of intraoperative technical problems which could have been solved had more time been taken with the procedure.

We will be the first to admit that we still have complications both during and following surgery and that some of these are technical in their genesis. However, intraoperative strokes attributable to inadequate cerebral protection or embolization through a functioning shunt have been reduced to well below 1% and postoperative internal carotid artery occlusions are most uncommon (less than .05%). The primary cause for neurological complications at this institution following surgery are complications related to hyperperfusion rather than hypoperfusion.

We do not know the exact circumstances that led other workers in this field to adopt a posture of routine...
shunting or some form of monitoring with selective shunting but we do know what persuaded us. Monitoring techniques were adopted over 10 years ago at this institution after the results of endarterectomy without monitoring were analyzed and found to be unacceptable. At that time our overall morbidity-mortality (not synonymous with complications as many complications do not result in morbidity if addressed promptly) was less than 5% but it related to a group of lower risk patients than are currently undergoing surgery at this institution. In spite of the fact that we seldom took more than 15 to 20 minutes for the arterial procedure itself, a number of patients awoke from surgery with either a major or a minor neurological deficit, some were transient, others permanent. Although ever cognizant of the risk of embolization, we did not feel that these deficits were attributable to that cause. Furthermore, we had a postoperative internal carotid artery occlusion rate approximating 3% in over 100 patients operated without patch grafting (the fortunate identification of the occlusion in two patients by a reduction in the postoperative retinal artery pressure measurement led to prompt reconstruction of the endarterectomy with patch grafting before the development of a neurological deficit). An agonizing reappraisal led to the decision to perform a more meticulous endarterectomy and patch graft more frequently. Coupled with this approach was the need to provide cerebral protection by indwelling shunts either routinely or selectively during the period of carotid occlusion as the period of occlusion would obviously be greater. Consideration was given to improving collateral flow by elevating the mean systemic blood pressure and recently this has been reported to be quite effective. However, this approach is not free of cardiac complications and is quite dependent on the adequacy of the collateral circulation.

Monitoring and Shunting During Surgery

From January 1972 through June 1982, we performed 1,456 endarterectomies for carotid stenosis using the intraoperative monitoring techniques previously described complemented by retinal artery pressure measurements postoperatively in all patients and more recently routine oculoplethysmography and digital subtraction angiography. The correlation of our cerebral blood flow measurements with electroencephalograms in these cases has been excellent and differs rather strikingly from the results in the 27 patients quoted by Dr. Ferguson. The lowest occlusion flow found by Dr. Ferguson in his 27 patients was 12 ml/100g/min. We have had 29 cases with occlusion flows between 0 and 4, 80 with flows between 5 and 9, and 159 with flows between 10 and 14 ml/100g/min. Using the xenon washout technique, flows below 5 are difficult to quantitate and can be equated essentially to zero flow. Thus we believe that 2% of the patients in our group would definitely have sustained a cerebral infarction without shunting because of inadequate collateral flow. Another 3–4%, that is patients with flows between 5 and 9 ml/100g/min, probably would have sustained an infarction with any prolonged period of occlusion. Patients with flows between 10 and 14, representing 10% of the group, may or may not have withstood the period of ischemia; this will be discussed below. Shunts were also used in a large number of patients with flows between 15 and 20 ml/100g/min for fear that the electroencephalogram would fail to reveal regions of focal ischemia in the deep white matter or basal ganglia with these borderline flows. Occasional patients with flows above 20 ml/100g/min were also shunted if they had a pre-existing electroencephalographic abnormality related to a preoperative infarct as we have found, as have others, that these patients are particularly vulnerable to marginal flow. Parenthetically, the shunts are not inserted until the plaque has been removed from the internal carotid artery except in those cases in which flow was below 5 ml/100g/min or in which there has been a dramatic and catastrophic change in the EEG (usually these are simultaneous events and one does not often occur without the other).

A grand total of 645 out of the 1,456 endarterectomies were protected with indwelling shunts during the operation. Embolic complications during the operation are easily identified by a very dramatic change in the electroencephalogram and thus we have hard data on the incidence of emboli. There were 5 cases of emboli through a functioning shunt during the operation. Three of these were related to proximal atherosclerosis and might possibly have been avoided, retrospectively, with more experience. The other emboli complications were minor and the patients regained a normal electroencephalogram prior to awakening from surgery and had normal neurological function in the recovery room. There were 9 cases of emboli during the exposure (some leading to a transient EEG change, others to a neurological complication) so that the risk of embolization is not limited to the placement or use of a shunt.

Changes in the electroencephalogram have mirrored the severity of reduction in cerebral blood flow during the period of occlusion. Furthermore, we have never had a patient awaken from anesthesia with a new neurological deficit that was not predicted by the electroencephalogram during the operation unless the patient had a major electroencephalographic abnormality prior to surgery related to an area of ischemia or infarction. Patients who were at high risk for surgery and who were considered neurologically unstable had significantly lower occlusion flows than did the other patients in the series. These patients also had lower baseline flows leading one to the conclusion that the microembolic and hemodynamic theories for transient ischemic attacks and infarctions are not mutually exclusive. Areas of brain functioning on a marginal flow of 40 to 50% of normal are particularly vulnerable to the effects of emboli.

Conversely, Whisnant found from a detailed multivariate analysis of a group of patients with transient
ischemic attacks operated in the period of 1970–1974 that no patients with a high occlusion flow had an intraoperative or postoperative stroke. Furthermore, this group had no stroke in 4.5 years of follow-up evaluation indicating that individuals with high collateral flow have a good prognosis.

Critical Flow and Ischemic Tolerance

The critical flow required to maintain a normal electroencephalogram may be higher than the critical flow required to maintain basic cell metabolism so that even with a state of physiological paralysis cell death is prevented and recovery is possible after a certain latency. We have found some biological variation in the critical flow to maintain a normal electroencephalogram and undoubtedly a biological variation exists for the critical flow required to maintain cell viability. Data from both our studies and the studies by Boylan et al show that the critical flow for the former ranges between 15 and 20 ml/100g/min and laboratory studies suggest that the critical flow for the latter in primates is between 10 and 15 ml/100g/min. It follows that the ischemic tolerance of neural tissue is proportional to both the duration and severity of flow reduction. The precise duration of time that these reduced flows can be tolerated before cellular injury occurs is unknown.

Intraoperative cerebral blood flow measurements using intra-arterially injected xenon are a great deal more reliable than blood flow measurements using the inhalation xenon technique in which the true severity of ischemic lesions are not identified. Using the intra-arterial injection technique a representative amount of indicator arrives in the area predestined for ischemia prior to occlusion of the vessel and thus measurements are based on the clearance of indicator from the true region of ischemia. With systemic administration of xenon, intravenous or inhalation, artifacts in these measurements develop related to "look-through" in which the blood flow probe measures from normally perfused tissue deep to the area of ischemia because the obstructions to the arterial in-flow prevent the indicator from arriving in the ischemic zone.

Cerebral blood flow measurements in the laboratory animal are difficult because of the small size of the brain studied and the even smaller areas of brain subjected to ischemia. Furthermore, the common laboratory animals, the dog, cat, and rat, have excellent collateral circulations over the cortex so that areas of ischemia often lie remote from the area of measurement. The primate unfortunately remains the only animal in which cerebral blood flow measurements comparable to those in the human can be acquired. In these animals it is very difficult to perform accurate measurement of cerebral blood flow throughout a period of prolonged ischemia and salvage that particular animal for a chronic preparation to determine the ultimate areas of infarction. Thus it is necessary to often extrapolate from one study to another and measure blood flow, energy metabolites, and zones of infarctions in different preparations and then cross correlate the results.

The squirrel monkey makes an excellent model for focal incomplete cerebral ischemia and our early studies on this subject suggested that the animals could tolerate a 60–70% reduction in cerebral blood flow for approximately one hour. This did not exclude microinfarctions as the non-uniform characteristics of flow in areas of incomplete ischemia were readily apparent in the microcirculation. During this time of incomplete ischemia there was a steady decrease in adenosine triphosphate and rise in lactate. However, these animals were operated under barbiturate anesthesia and at that time we did not understand the protective effects of this agent. Thus this period of one hour might be a good bit shorter in the awake animals and studies by other investigators suggested that this was indeed the case.

During the period of the above investigations (1965–1972) it was our belief that seldom, if ever, would cerebral blood flow fall below a critical level of cell viability during carotid endarterectomy as collateral flow from one source or another would be able to sustain at least a flow of 10 to 15 ml/100g/min, particularly if the patient were protected with an elevated blood pressure. With greater experience, as indicated above, we found that this indeed was not the case. In some patients hemispheric blood flow falls to essentially zero with carotid occlusion approximating quite closely the situation of cardiac arrest or animal decapitation in which both clinical experience and laboratory data suggest that within 4 to 9 minutes of zero flow irreparable brain damage begins to occur.

The laboratory confirmation of the clinical impressions had to await the elegant studies of Symon et al in the Rhesus monkey. This group established that blood flows below 15 ml/100g/min result in a paralysis of neuronal activity and that flows below 10 ml/100g/min result in ionic shifts that may be irreversible if allowed to persist. The true level of tolerance for ischemia in patients who have flows between 5 and 10 or between 10 and 15 ml/100g/min is unknown, but recent studies stress the variability and futility of histological changes at these levels. We prefer not to speculate how long a particular person can retain a physiological paralysis without developing neuronal damage. There is some recent evidence that incomplete ischemia, which is associated with a greater degree of acidosis than is complete ischemia because of the continued glycolysis in the former state that is absent in the latter, has complications uniquely related to its acidosis.

Skillful General Anesthesia

Possibly the most sensitive monitor of neurological function is the awake patient and some very experienced surgeons still use this method of monitoring. Like Dr. Ferguson, we prefer general anesthesia as it is amazingly safe in the hands of competent anesthesiologists, protects the patient's airway, facilitates high
exposures of distal internal carotid artery lesions, and in general not only improves the comfort of the patient but also that of the surgeon. However, to date, barbiturates are the only anesthetic agents that have unequivocally been proven to protect the brain and improve the tissue tolerance to ischemia. Our recent experience suggests that the critical flow does seem to be lower with isoﬂuorane but these are only preliminary data. Data from Michenfelder’s laboratory suggest that this may be a valid observation.

Short Occlusion Time

In our judgment a rapid endarterectomy is fraught with hazard. The plaque must be removed meticulously from the vessel with no lip of intima distally to serve as a source of dissection and no stump of the external carotid artery to serve as a source of emboli. In our experience the best reconstruction of the vessel is achieved with a saphenous vein patch graft which extends the period of occlusion approximately 15 minutes. The only series to date of patients operated without patch angioplasty routinely undergoing postoperative angiograms (by an experienced and respected group) is reported to demonstrate a 20% occlusion rate of the external carotid artery and a 4% occlusion rate of the internal carotid artery.

Hyperperfusion Syndromes

Our most common complication following endarterectomy is related to the group of high risk patients in which there has been a very marked increase in cerebral blood flow during the operative procedure. These usually occur several days after surgery in patients who had a low baseline cerebral blood flow measurement before endarterectomy and had a 200% increase (or more) of flow following endarterectomy. This paralysis of autoregulation leads to an ipsilateral hemispheric hyperperfusion and associated vascular headaches. Fortunately, in most patients, this seems to be limited to unilateral headache. However, in some patients it has been associated with paroxysmal lateralizing epileptiform discharges, cerebral hemorrhage, and migraine variants. Most all of these patients, except those with headaches alone, have undergone angiography at the time of the complication and in none of them have we identified major intracranial vessel occlusions. Hemorrhage into an area of previous infarction is a well-known complication of endarterectomy. However, these hyperperfusion syndromes have occurred in patients without a major area of infarction. These types of complications have only been infrequently reported leading us to the concern that they might be uniquely related to our policy of not reversing the heparin given at surgery, a policy based on the protective effects of heparin on the thrombogenic surface of a freshly endarterectomized vessel. Alternatively, lacking cerebral blood flow monitoring, these complications might not be recognized as unique by other groups and attributed to a different mechanism.

Closing Comments

Experience can be defined as a compilation of one’s complications. Experience of most of the outstanding pioneers in this field led them to conclude that routine shunting or some form of monitoring (an awake patient or internal carotid artery back pressure) with selective shunting was advisable. It was the experience of these individuals that a number of complications occurred which could not be attributed to embolic events. Those of us who are now second generation surgeons and who shared the disappointments of their first generation mentors vividly recall certain types of complications which were frequent enough that they were not anecdotal. One of these, in patients operated under local anesthesia, was the onset of an acute and profound hemiplegia with carotid occlusion that was irreversible with restoration of flow 20 to 30 minutes thereafter.

Constructive criticism and thoughtful analyses are healthy and essential for progress. However, it behooves us to be cautious and prudent before we discard general practices on the basis of a relatively few number of cases and thereafter have a third generation of surgeons necessarily undergo an entirely new learning experience all over again at considerable expense and morbidity to our patients.

There is no room for a cavalier attitude toward carotid endarterectomy. It can be a relatively easy operation or an extremely difficult procedure. In either case, the relatively simple or the complex, it remains a dangerous operation with intraoperative risks of embolization and/or infarction from inadequate flow during the period of occlusion and postoperative risks of occlusion or embolization from vessels inadequately reconstructed or from complications of cerebral hyperperfusion following the restoration of a normal perfusion pressure to a vascular bed with paralyzed autoregulation.

References

9. Easton JD, Sherman DG: Stroke and mortality rate in carotid endarterectomy: 228 consecutive operations. Stroke 8: 565-568,
52. Michenfelder JD, Theye RA: The effects of anesthesia and hypothermia on canine cerebral ATP and lactate during anoxia produced by decapitation. Anesthesiology 33: 430–439, 1970
59. Michenfelder JD: The interdependency of cerebral functional and metabolic effects following massive doses of thiopental in the dog. Anesthesiology 41: 231–236, 1974
60. Michenfelder JD, Theye RA: Cerebral protection by thiopental during hypoxia. Anesthesiology 39: 510–517, 1973
61. Michenfelder JD, Theye RA: Effects of fentanyl, droperidol, and ...

62. Michenfelder JD: Personal Communication, 1982


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